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In re Application of:

Hott, J.S. et al.

Serial No.: 10/005,512

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For: **An Immunotoxin (mAB-RICIN)
for the Treatment of Focal
Movement Disorders**

Examiner: Nolan, P.J.

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Information Disclosure Statement Pursuant to 37 C.F.R. § 1.97(b)(1)

Honorable Director of Patents
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Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. Copies of documents AS1, AR2, AT4, AT5, AS6, AT7, AR8, AS8, and AS9 are enclosed. Copies of all other documents may be found in the files of U.S. Patent Application Serial No. 09/418,854 (filed: October 15, 1999) or U.S. Patent Application Serial No. 08/937, 266 (filed: September 15, 1997).

This Information Disclosure Statement is being submitted prior to an Initial Office Action on the merits. No fee is accordingly believed due for consideration of this Information Disclosure Statement. However, if the Commissioner determines that a fee is required in for consideration of this Information Disclosure Statement, the U.S. Patent and Trademark Office is hereby authorized to

charge any fee deficiency, or credit any overpayment, to Deposit Account No. 50-0548 referencing docket number 3514. Youle

The submitted documents are:

- AA1 U.S. Patent No. 5,183,462 (Borodic, G.E.)
- AB1 U.S. Patent No. 5,239,062 (Blattler *et al.*)
- AC1 U.S. Patent No. 5,562,907 (Arnon, S.S.)
- AD1 U.S. Patent No. 5,721,215 (Aoki, K.R. *et al.*)
- AL1 EP Application 0 770 395 A1
- AR1 Appel, S.H. *et al.*, "Accelerated degradation of acetylcholine receptor from cultured rat myotubes with myasthenia gravis sera and globulins," Proc Natl Acad Sci U S A. 1977 May;74(5):2130-4
- AS1 Barbet, J. *et al.*, "Specific Toxicity to Activated T and B Lymphocytes of a Ricin A Immunotoxin Directed Against the Class I MHC Antigen H-2 K" Antibody, Immunoconj. Radiopharmaceuticals 1(2):169-180 (1988)
- AT1 Borodic, G. *et al.*, "Botulinum toxin therapy, immunologic resistance, and problems with available materials," Neurology. 1996 Jan;46(1):26-9
- AR2 Christiansen, S.P. *et al.* "Acute effects of the skeletal muscle-specific immunotoxin ricin-mAb 35 on extraocular muscles of rabbits," Invest Ophthalmol Vis Sci. 2000 Oct;41(11):3402-9
- AS2 Clementi, F. *et al.*, "Acetylcholine receptor degradation: study of mechanism of action of inhibitory drugs," Eur J Cell Biol. 1983 Jan;29(2):274-80
- AT2 Clementi, F. *et al.*, "Antibody induced internalization of acetylcholine nicotinic receptor: kinetics, mechanism and selectivity," Eur J Cell Biol. 1985 May;37:220-8
- AR3 de la Cruz, R.R. *et al.*, "Behavior of cat abducens motoneurons following the injection of toxic ricin into the lateral rectus muscle," Brain Res. 1991 Mar 29;544(2):260-8

- AS3 de la Cruz, R.R. *et al.*, "Effects of target depletion on adult mammalian central neurons: functional correlates," *Neuroscience*. 1994 Jan;58(1):81-97
- AT3 de la Cruz, R.R. *et al.*, "Neurotoxic lesion of oculomotor neurons: evidence for rearrangement of axon terminals of surviving afferent neurons," *Neurotoxicology*. 1994 Fall;15(3):633-6
- AR4 de la Cruz, R.R. *et al.*, "Response of adult cat abducens internuclear interneurons to selective removal of their target motoneurons," *Exp Brain Res*. 1991;84(1):167-72
- AS4 Gardner, J.M. *et al.*, "Acetylcholine receptor degradation measured by density labeling: effects of cholinergic ligands and evidence against recycling," *Cell*. 1979 Mar;16(3):661-74
- AT4 Goldmacher, V.S. *et al.*, "The specific cytotoxicity of immunoconjugates containing blocked ricin is dependent on the residual binding capacity of blocked ricin: evidence that the membrane binding and A-chain translocation activities of ricin cannot be separated," *Biochem Biophys Res Commun*. 1992 Mar 16;183(2):758-66
- AR5 Greenfield, L. *et al.*, "Mutations in diphtheria toxin separate binding from entry and amplify immunotoxin selectivity," *Science*. 1987 Oct 23;238(4826):536-9.
- AS5 Griffin, T.W. *et al.*, "Chimeras, Castor Beans and Cancer: Antibody and Ligand-Toxin Conjugates as Therapeutic Agents," In: *Cancer Therapy in the Twenty-First Century: Molecular and Immunologic Approaches*, Futura Publishing Co., Inc., Mt. Kisco, NY 1994
- AT5 Grossbard, M.L. *et al.*, "Correlation between in vivo toxicity and preclinical in vitro parameters for the immunotoxin anti-B4-blocked ricin," *Cancer Res*. 1992 Aug 1;52(15):4200-7
- AR6 Holds, John B. *et al.*, "Botulinum A toxin injection. Failures in clinical practice and a biomechanical system for the study of toxin-induced paralysis," *Ophthal Plast Reconstr Surg*. 1990;6(4):252-9
- AS6 Leonard, J.E. *et al.*, "Kinetics of protein synthesis inactivation in human T-lymphocytes by selective monoclonal antibody-ricin conjugates," *Cancer Res*. 1985 Nov;45(11 Pt 1):5263-9
- AT6 Loutrari, H. *et al.*, "Use of Torpedo-mouse hybrid acetylcholine receptors reveals immunodominance of the alpha subunit in myasthenia gravis antisera," *Eur J Immunol*. 1992 Nov;22(11):2949-56
- AR7 Moreno-Lopez, B. *et al.*, "Botulinum neurotoxin alters the discharge characteristics of abducens motoneurons in the alert cat," *J Neurophysiol*. 1994 Oct;72(4):2041-4

- AS7 Printseva, O. *et al.*, "Selective killing of smooth muscle cells in culture by the ricin A-chain conjugated with monoclonal antibodies to a cell surface antigen via a dextran bridge," *Experientia*. 1985 Oct 15;41(10):1342-4
- AT7 Vitetta, E.S. *et al.* "Synergy of ricin A chain-containing immunotoxins and ricin B chain-containing immunotoxins in in vitro killing of neoplastic human B cells," *Proc Natl Acad Sci U S A*. 1983 Oct;80(20):6332-5
- AR8 Weil-Hillman, G. *et al.*, "Combined immunochemotherapy of human solid tumors in nude mice," *Cancer Res*. 1987 Jan 15;47(2):579-85
- AS8 Weil-Hillman, G. *et al.*, "Cytotoxic effect of anti-Mr 67,000 protein immunotoxins on human tumors in a nude mouse model," *Cancer Res*. 1985 Mar;45(3):1328-36
- AT8 Wiley, R.G., "Neural lesioning with ribosome-inactivating proteins: suicide transport and immunolesioning" *Trends Neurosci*. 1992 Aug;15(8):285-90
- AR9 Youle, R.J. *et al.*, "Role of Endocytosis and Receptor Recycling in Ligand-Toxin and Antibody-Toxin Conjugate Activity," In: *Immunoconjugates. Antibody Conjugates in Radioimaging and Therapy of Cancer* (C.-W. Vogel, Ed.) New York, Oxford University Press, pp. 153-169
- AS9 Youle, R.J. *et al.*, "Studies on the galactose-binding site of ricin and the hybrid toxin Man6P-ricin," *Cell*. 1981 Feb;23(2):551-9

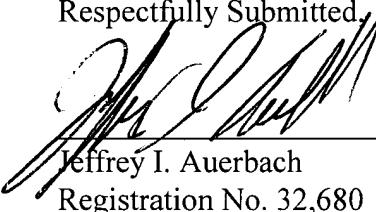
The submission of the listed and appended documents is not intended as an admission that any such document constitutes prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

Applicants respectfully request that the documents listed on the accompanying Form PTO 1449 be considered and made of record in the present application. Applicants further request that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

While the listed references are considered relevant to the prosecution of the present application, it is submitted that the references, either alone or in combination, do not detract from the patentability of the claimed invention.

Date: 4/23/2003
Liniak, Berenato & White, LLC
6550 Rock Spring Drive, Suite 240
Bethesda, MD 20817 Reg. No. 32,680
Telephone: (301) 896-0600
Facsimile: (301) 896-0607

Respectfully Submitted,



Jeffrey I. Auerbach
Registration No. 32,680
Attorney for Assignee